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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,335	11/13/2003	Adolfo J. De Bold	14703-002001	1171

26161 7590 05/28/2010

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
05/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/712,335	DE BOLD, ADOLFO J.	
	Examiner	Art Unit	
	VANESSA L. FORD	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,20 and 24* is/are pending in the application.

4a) Of the above claim(s) *22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,20 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. Applicant's amendment and response filed February 22, 2010 are acknowledged. Claims 1-2 have been amended. Claim 24 had been added.

Claim 22 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 26, 2006.

Claims 1-13, 20 and 24 are under examination.

Rejections Withdrawn

2. In view of Applicant's amendment and remarks the following rejections are withdrawn:

(a) rejection of claims 1-3, 8, 13 and 30 under 35 U.S.C.102(b), pages 5-7, paragraph 5.

(b) rejection of claims 1-4, 8, 11-13 and 20 under 35 U.S.C. 103(a), pages 7-10, paragraph 6.

(c) rejection of claims 1-3, 5, 8, 11-13 and 20 under 35 U.S.C. 103(a), pages 11-14, paragraph 7.

(d) rejection of claims 1-3, 6-9, 11-13 and 20 under 35 U.S.C. 103(a), pages 14-18, paragraph 8.

(e) rejection of claim 10 under 35 U.S.C. 103(a), pages 18-20, paragraph 9.

Rejection Maintained

The following rejection is maintained and reiterated below:

3. The rejection under 35 U.S.C. 102 (a) is maintained for claims 1-3, 6-9, 13, 20 and newly submitted claim 24 for the reasons set forth on pages 4-5, paragraph 4 of the previous Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The claims are rejected under 35 U.S.C. 102(a) is anticipated by Ribeiro et al *(The Lancet, August 10, 2002, Vol. 360, p. 461-462).*

Independent claim 1 is directed a method of predicting whether a human patient is susceptible to cardiomyopathy, myocarditis or both, resulting from in an infection, the method comprising obtaining a sample of a body fluid from the patient, and determining a level of a brain natriuretic peptide (BNP) or both BNP and atrial natriuretic peptide (ANF) within the sample of body fluid and comparing the level of BNP or both BNP and ANF to the level of BNP or both BNP and ANF from a control group, wherein an increase in the level of BNP or both BNP and ANF in the sample, compared to the level of BNP or both BNP and ANF in the control group, is an indicator that cardiomyopathy, myocarditis or both cardiomyopathy and mycarditis will arise as a result of an infection in the patient and predicting the patient is susceptible to cardiomyopathy, myocarditis, or both as a result of the infection where the level of BNP or both BNP and ANF in the sample is increased.

Dependent claim 6 is directed to the method of claim 1 wherein the infection comprises a viral infection, a rickettsial infection, a bacterial infection, a mycobacterial infection, a spirochetal infection, a fungal infection or a parasitic infection.

Dependent claim 7 is directed to the method of claim 6 wherein the parasitic infection comprises *Trypanosoma cruzi.*

Dependent claim 8 is directed to the method of claim 2, wherein at least one antibody comprises a polyclonal antibody, a monoclonal antibody or combination thereof.

Ribeiro et al teach a method of predicting whether a patient has cardiomyopathy comprising analyzing the BNP levels of Chagas' disease patients. Ribeiro et al teach that plasma samples of the patients used in the study were analyzed for BNP level (see page 461). Ribeiro et al teach that a radioimmunoassay using specific human antibody was used to analyze BNP levels (page 461). Ribeiro et al teach that Chagas' patients with high plasma concentrations of BNP in association with impaired left ventricular function (page 462). Ribeiro et al teach that high BNP concentrations can accurately identify patients who have an echocardiographic investigation (page 462). Ribeiro et al teach that since Chagas' disease patients with a normal electrocardiogram and chest radiograph are unlikely to have reduced left ventricular ejection fraction (LVEF) and BNP measurement could be especially, useful in those of abnormal electrocardiogram or chest radiograph (page 462). Ribeiro et al teach that early recognition of patients with low LVEF could allow the use of drugs which and delay the progression of left ventricular dysfunction and reduce mortality (page 462).

Ribeiro et al anticipate the claimed invention.

Applicant's Arguments

Applicant urges that Ribeiro et al there is no reference to cardiomyopathy or myocarditis, so that the Office surmises that left ventricle dysfunction (LVD) is equivalent to cardiomyopathy or myocarditis. Applicant urges that LVD with subsequent congestive heart failure constitutes the final stage for a host of cardiac disorders including cardiomyopathy or myocarditis. Applicant urges that LVD does not necessarily suffer from cardiomyopathy or myocarditis. Applicant urges that Riberio et al do not describe cardiomyopathy or myocarditis or associate an elevated BNP level in Chagas disease with cardiomyopathy or myocarditis and therefore does not anticipate the present claims.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed February 22, 2010 have been fully considered but they are not persuasive. The claims are drawn to a method of predicting *whether a human patient is susceptible to cardiomyopathy*, myocarditis or both, resulting from in an infection. Ribeiro et al teach a method of predicting whether a patient has cardiomyopathy comprising analyzing the BNP levels of Chagas' disease patients. Ribeiro et al teach the claimed invention because they suggest that BNP assays may have major clinical indications in areas where Chagas is a cause of heart failure (page 3). Thus, Riberio et al anticipate the claimed invention.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-4, 8, 11-13, 20 and newly submitted claim 24 under 35 U.S.C. 103(a) unpatentable over Ribeiro et al *(The Lancet, August 10, 2002, Vol. 360, p. 461-462)* in view of Arad et al *(Cardiology, 1996; 87:12-17)* and further in view of Totsune et al *(Regul. Pept, 1996, Jul., 5;63(2-3):141-7).*

Independent claim 1 is directed a method of predicting whether cardiomyopathy, myocarditis or both, will rise as a result of an infection in a human patient, the method comprising obtaining a sample of a body fluid from the patient, and determining a level of a brain natriuretic peptide (BNP) or both BNP and atrial natriuretic peptide (ANF) within the sample of body fluid and comparing the level of BNP or both BNP and ANF to the level of BNP or both BNP and ANF from a control group, wherein an increase in the level of BNP or both BNP and ANF in the sample, compared to the level of BNP or both BNP and ANF in the control group, is an indicator that cardiomyopathy, mycarditis or both cardiomyopathy and mycarditis will arise as a result of an infection in the patient.

Dependent 4 is directed to the method of claim 1 wherein the body fluid comprises urine.

Dependent claim 11 is directed the method of claim 2 wherein the step of obtaining a sample of a body fluid from the patient comprises obtaining two or more samples of body fluid from the patient at different points in time.

Dependent claim 12 is directed to the method of claim 11 wherein, in the step determining the level of BNP or the level BNP and ANF, the level of BNP or the level of BNP and ANF is determined within each of the two or more samples of body fluid and the level of BNP of both BNP and ANF compared to determine a change in the BNP or both BNP and ANF levels within the body fluid over time.

Ribeiro et al teach a method of predicting whether a patient has cardiomyopathy comprising analyzing the BNP levels of Chagas' disease patients. Ribeiro et al teach that plasma samples of the patients used in the study were analyzed for BNP level (see

page 461). Ribeiro et al teach that a radioimmunoassay using specific human antibody was used to analyze BNP levels (page 461). Ribeiro et al teach that Chagas' patients with high plasma concentrations of BNP in association with impaired left ventricular function (page 462). Ribeiro et al teach that high BNP concentrations can accurately identify patients who have an echocardiographic investigation (page 462). Ribeiro et al teach that since Chagas' disease patients with a normal electrocardiogram and chest radiograph are unlikely to have reduced left ventricular ejection fraction (LVEF) and BNP measurement could be especially, useful in those of abnormal electrocardiogram or chest radiograph (page 462). Ribeiro et al teach that early recognition of patients with low LVEF could allow the use of drugs which and delay the progression of left ventricular dysfunction and reduce mortality (page 462).

Ribeiro et al do not teach atrial natriuretic peptides (ANP).

Arad et al teach that both BNP and ANP seem to be related to ventricular dysfunction (page 12). Arad et al teach that ANP plasma levels stand in a well-established correlation with the severity of heart failure (page 12). Arad et al suggest that BNP may also be a marker for ventricular myocardial pathology (page 15).). Arad et al teach that plasma BNP and ANP levels were analyzed in patients without symptoms or signs of heart failure (Group AP) or with severe heart failure due to ischemic heart disease (Group HF) (page 13). Arad et al teach based on S.S. patient's elevated BNP levels (133 pg/ml, ANP 78 pg/ml) that this patient was in compensated heart failure (page 15). Arad et al teach that the plasma BNP and ANP levels were assessed using a radioimmunology assay (page 13). Thus, the prior inherently teaches that the

concentration of BNP is determined by at least one antibody with affinity to BNP, ANP or both. Arad et al teach that BNP has several characteristics suggesting that it might be a better marker of ventricular myocardial pathology than ANP (page 15). Arad et al teach that the ratio of ventricular to atrial contribution to BNP secretion is higher than that of ANP in the basal state (42% vs. 2.2%) (page 16) and is especially elevated in the course of development of heart failure (108 vs. 14%), respectively. Arad et al teach that the plasma half-life of BNP is longer than that of ANP. Thus, making it ANP less susceptible to instantaneous changes in heart rate, preload and afterload (page 16). Arad et al disclose that BHP is elevated in systolic and diastolic ventricular dysfunction, posttransplantation and in acute mycocardial infarction (page 16). Arad et al teach that both hormones (BNP and ANP) were elevated and highly correlated one with the other in patients with predominantly systolic dysfunction (page 17). Arad et al teach that BNP and ANP levels in patients without heart failure and in controls subjects were low (page 17). Arad et al teach that abnormal BNP levels are a useful marker of heart dysfunction and should not be overlooked (page 17).

Riberio et al and Arad et al do not teach the claim limitation "wherein the body fluid comprises urine".

Totsune et al teach that atrial natriuretic peptide (ANP) is present in the urine (see the Abstract).

It would have been *prima facie* obvious at the time the invention was made to substitute the body fluid sample, plasma for the body fluid sample, urine in a method of assisting in the of cardiomyopathy, myocarditis or both, that arises as a result of an

infection in a patient because Totsune et al teach that atrial natriuretic peptide (ANP) is present in the urine. It would be expected, absent evidence to the contrary, that a urine sample would be an appropriate sample to test for the presence of atrial natriuretic peptides or brain natriuretic peptides.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one composition and a person of ordinary skill would recognize that it would be used in similar compositions in the same way, using the technique is obvious unless its application is beyond that person's skill. Thus, it would be obvious to use a known products from known sources in a method of diagnosis cardiomyopathy, myocarditis or both that is ready for improvement to yield predictable results.

5. Claims 1-3, 5-13 and 20 are rejected under 35 U.S.C. 103(a) as unpatentable over Ribeiro et al *(The Lancet, August 10, 2002, Vol. 360, p. 461-462)* in view of Arad et al *(Cardiology, 1996; 87:12-17)* and further in view of Kaneko et al *(Brain Res, May 28, 1993; 612(1-2):104-9)(Abstract only).*

Independent claim 1 is directed a method of predicting whether cardiomyopathy, myocarditis or both, will rise as a result of an infection in a human patient, the method comprising obtaining a sample of a body fluid from the patient, and determining a level of a brain natriuretic peptide (BNP) or both BNP and atrial natriuretic peptide (ANF) within the sample of body fluid and comparing the level of BNP or both BNP and ANF to the level of BNP or both BNP and ANF from a control group, wherein an increase e in

the level of BNP or both BNP and ANF in the sample, compared to the level of BNP or both BNP and ANF in the control group, is an indicator that cardiomyopathy, mycarditis or both cardiomyopathy and mycarditis will arise as a result of an infection in the patient.

Dependent 5 is directed to the method of claim 1 wherein the body fluid comprises cerebrospinal fluid.

Dependent claim 11 is directed the method of claim 2 wherein the step of obtaining a sample of a body fluid from the patient comprises obtaining two or more samples of body fluid from the patient at different points in time.

Dependent claim 12 is directed to the method of claim 11 wherein, in the step determining the level of BNP or the level BNP and ANF, the level of BNP or the level of BNP and ANF is determined within each of the two or more samples of body fluid and the level of BNP of both BNP and ANF compared to determine a change in the BNP or both BNP and ANF levels within the body fluid over time.

Ribeiro et al teach a method of predicting whether a patient has cardiomyopathy comprising analyzing the BNP levels of Chagas' disease patients. Ribeiro et al teach that plasma samples of the patients used in the study were analyzed for BNP level (see page 461). Ribeiro et al teach that a radioimmunoassay using specific human antibody was used to analyze BNP levels (page 461). Ribeiro et al teach that Chagas' patients with high plasma concentrations of BNP in association with impaired left ventricular function (page 462). Ribeiro et al teach that high BNP concentrations can accurately identify patients who have an echocardiographic investigation (page 462). Ribeiro et al teach that since Chagas' disease patients with a normal

electrocardiogram and chest radiograph are unlikely to have reduced left ventricular ejection fraction (LVEF) and BNP measurement could be especially, useful in those of abnormal electrocardiogram or chest radiograph (page 462). Ribeiro et al teach that early recognition of patients with low LVEF could allow the use of drugs which and delay the progression of left ventricular dysfunction and reduce mortality (page 462).

Ribeiro et al do not teach atrial natriuretic peptides (ANP).

Arad et al teach that both BNP and ANP seem to be related to ventricular dysfunction (page 12). Arad et al teach that ANP plasma levels stand in a well-established correlation with the severity of heart failure (page 12). Arad et al suggest that BNP may also be a marker for ventricular myocardial pathology (page 15).). Arad et al teach that plasma BNP and ANP levels were analyzed in patients without symptoms or signs of heart failure (Group AP) or with severe heart failure due to ischemic heart disease (Group HF) (page 13). Arad et al teach based on S.S. patient's elevated BNP levels (133 pg/ml, ANP 78 pg/ml) that this patient was in compensated heart failure (page 15). Arad et al teach that the plasma BNP and ANP levels were assessed using a radioimmunology assay (page 13). Thus, the prior inherently teaches that the concentration of BNP is determined by at least one antibody with affinity to BNP, ANP or both. Arad et al teach that BNP has several characteristics suggesting that it might be a better marker of ventricular myocardial pathology than ANP (page 15). Arad et al teach that the ratio of ventricular to atrial contribution to BNP secretion is higher than that of ANP in the basal state (42% vs. 2.2%) (page 16) and is especially elevated in the course of development of heart failure (108 vs. 14%), respectively. Arad et al teach

that the plasma half-life of BNP is longer than that of ANP. Thus, making it ANP less susceptible to instantaneous changes in heart rate, preload and afterload (page 16). Arad et al disclose that BHP is elevated in systolic and diastolic ventricular dysfunction, posttransplantation and in acute mycocardial infarction (page 16). Arad et al teach that both hormones (BNP and ANP) were elevated and highly correlated one with the other in patients with predominantly systolic dysfunction (page 17). Arad et al teach that BNP and ANP levels in patients without heart failure and in controls subjects were low (page 17). Arad et al teach that abnormal BNP levels are a useful marker of heart dysfunction and should not be overlooked (page 17).

Riberio et al and Arad et al do not teach the claim limitation "wherein the body fluid comprise “cerebrospinal fluid”.

Kaneko et al teach that atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are present in human cerebrospinal fluid and can be by specific radioimmunoassay (see the Abstract).

It would have been *prima facie* obvious at the time the invention was made to substitute the body fluid sample, plasma as taught by Riberio et al and Arad et al as combined for the body fluid sample, cerebrospinal fluid as taught by Kaneko et al in a method of predicting whether of cardiomyopathy, myocarditis or both, that will arise as a result of an infection in a patient because Kaneko et al teach that atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are present in human cerebrospinal fluid and can be by specific radioimmunoassay. It would be expected, absent evidence

to the contrary, that a cerebrospinal fluid sample would be an appropriate sample to test for the presence of ANP and BNP.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one composition and a person of ordinary skill would recognize that it would be used in similar compositions in the same way, using the technique is obvious unless its application is beyond that person's skill. It is well known in the art that elevated levels of ANP and BNP are associated with cardiomyopathy or heart failure. It is well known in the art to that cerebrospinal fluid is a source of atrial natriuretic peptides and brain natriuretic peptides. Thus, it would be obvious to use a known products from known sources in a method of diagnosis cardiomyopathy, myocarditis or both that is ready for improvement to yield predictable results.

6. Claims 1- 3, 6-13 and newly submitted 24 are rejected under 35 U.S.C. 103(a) as unpatentable over Ribeiro et al *(The Lancet, August 10, 2002, Vol. 360, p. 461-462)* in view of Arad et al *(Cardiology, 1996; 87:12-17)* and further in view of Mischak et al *(WO 97/32900 published September 12, 1997).*

Dependent claim 10 is directed to the method of claim 8 wherein at least one antibody comprises a monoclonal antibody.

Ribeiro et al teach a method of predicting whether a patient has cardiomyopathy comprising analyzing the BNP levels of Chagas' disease patients. Ribeiro et al teach that plasma samples of the patients used in the study were analyzed for BNP level (see page 461). Ribeiro et al teach that a radioimmunoassay using specific human antibody was used to analyze BNP levels (page 461). Ribeiro et al teach that Chagas' patients with high plasma concentrations of BNP in association with impaired left ventricular function (page 462). Ribeiro et al teach that high BNP concentrations can accurately identify patients who have an echocardiographic investigation (page 462). Ribeiro et al teach that since Chagas' disease patients with a normal electrocardiogram and chest radiograph are unlikely to have reduced left ventricular ejection fraction (LVEF) and BNP measurement could be especially, useful in those of abnormal electrocardiogram or chest radiograph (page 462). Ribeiro et al teach that early recognition of patients with low LVEF could allow the use of drugs which and delay the progression of left ventricular dysfunction and reduce mortality (page 462).

Ribeiro et al do not teach atrial natriuretic peptides (ANP).

Arad et al teach that both BNP and ANP seem to be related to ventricular dysfunction (page 12). Arad et al teach that ANP plasma levels stand in a well-established correlation with the severity of heart failure (page 12). Arad et al suggest that BNP may also be a marker for ventricular myocardial pathology (page 15).). Arad et al teach that plasma BNP and ANP levels were analyzed in patients without symptoms or signs of heart failure (Group AP) or with severe heart failure due to ischemic heart disease (Group HF) (page 13). Arad et al teach based on S.S. patient's elevated BNP levels (133 pg/ml, ANP 78 pg/ml) that this patient was in compensated heart failure (page 15). Arad et al teach that the plasma BNP and ANP levels were assessed using a radioimmunology assay (page 13). Thus, the prior inherently teaches that the concentration of BNP is determined by at least one antibody with affinity to BNP, ANP or both. Arad et al teach that BNP has several characteristics suggesting that it might be a better marker of ventricular myocardial pathology than ANP (page 15). Arad et al teach that the ratio of ventricular to atrial contribution to BNP secretion is higher than that of ANP in the basal state (42% vs. 2.2%) (page 16) and is especially elevated in the course of development of heart failure (108 vs. 14%), respectively. Arad et al teach that the plasma half-life of BNP is longer than that of ANP. Thus, making it ANP less susceptible to instantaneous changes in heart rate, preload and afterload (page 16). Arad et al disclose that BHP is elevated in systolic and diastolic ventricular dysfunction, posttransplantation and in acute mycocardial infarction (page 16). Arad et al teach that both hormones (BNP and ANP) were elevated and highly correlated one with the other in patients with predominantly systolic dysfunction (page 17). Arad et al teach that

BNP and ANP levels in patients without heart failure and in controls subjects were low (page 17). Arad et al teach that abnormal BNP levels are a useful marker of heart dysfunction and should not be overlooked (page 17).

The teachings of Ribeiro et al and Arad et al do not teach the claim limitation "wherein at least one antibody comprises a monoclonal antibody".

Mischak et al teach monoclonal antibodies that are used in immunoassays of the invention (page 3). Mischak et al teach reagents and assays for the quantification of human brain natriuretic peptide (hBMP) in plasma or serum (see the Abstract). Mischak et al teach that antibodies are provided which are monospecific to epitopes of hBNP (see the Abstract). Mischak et al teach that these antibodies and peptide fragments can be used in immunoassays using a sandwich format or a competition format (see the Abstract.

It would have been *prima facie* obvious at the time the invention was made to modify the method of predicting whether cardiomyopathy, myocarditis or both will arise as a result of an infection in a human patient as combined above comprising monoclonal antibodies to determining the BNP levels in patients because Arad et al teach that both hormones (BNP and ANP) were elevated and highly correlated one with the other in patients with predominantly systolic dysfunction and Arad et al teach that BNP has several characteristics suggesting that it might be a better marker of ventricular myocardial pathology than ANP; (a) the ratio of ventricular to atrial contribution to BNP secretion is higher than that of ANP in the basal state (42% vs. 2.2%) and is especially elevated in the course of development of heart failure (108 vs.

14%), respectively and (b) Arad et al teach that the plasma half-life of BNP is longer than that of ANP.

Moreover, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one composition and a person of ordinary skill would recognize that it would be used in similar compositions in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results". Thus, it would be obvious to use a known products from known sources in a method of diagnosis cardiomyopathy, myocarditis or both that is ready for improvement to yield predictable results.

Status of Claims

7. No claims allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to VANESSA L. FORD whose telephone number is (571)272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0756. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Vanessa L. Ford/

Primary Examiner, Art Unit 1645

May 23, 2010